

1 **Claims**

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3 1. Use of

4 (a) a specific binding member which binds to a
5 cell death receptor or a nucleic acid encoding
6 said binding member and7 (b) a chemotherapeutic agent, wherein the
8 chemotherapeutic agent is a topoisomerase
9 inhibitor or a thymidylate synthase inhibitor
10 in the preparation of a medicament for the
11 treatment of a cancer, wherein the cancer is a
12 cancer associated with a p53 mutation.

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14 2. The use according to claim 1 wherein the cancer
15 is one or more of colorectal, breast, ovarian,
16 cervical, gastric, lung, liver, skin and
17 myeloid (e.g. bone marrow) cancer.

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19 3. The use according to claim 1 or claim 2 wherein
20 the death receptor is FAS.

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22 4. The use according to claim 1 or claim 2 wherein
23 the binding member is an antibody or a fragment
24 thereof.

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26 5. The use according to any one of the preceding
27 claims wherein the binding member is the anti-
28 FAS antibody CH11.

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30 6. The use according to any one of the preceding
31 claims wherein said chemotherapeutic agent is
32 an antifolate thymidylate synthase inhibitor or

1 a topoisomerase-I inhibitor.

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3 7. The use according to any one of the preceding
4 claims, wherein said chemotherapeutic agent is
5 TDX or irinotecan (CPT-11).

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7 8. The use according to any one of the preceding
8 claims, wherein said specific binding member
9 and chemotherapeutic agent are provided in
10 concentrations sufficient to produce an RI of
11 greater than 1.5.

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13 9. A method of killing cancer cells having a p53
14 mutation, said method comprising the separate,
15 sequential or simultaneous administration to
16 said cells of a therapeutically effective
17 amount of a) a specific binding member which
18 binds to a cell death receptor or a nucleic
19 acid encoding said binding member and (b) a
20 chemotherapeutic agent, wherein said
21 chemotherapeutic agent is a topoisomerase
22 inhibitor or a thymidylate synthase inhibitor.

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24 10. A method of treating cancer cells having a p53
25 mutation comprising the separate, sequential or
26 simultaneous administration to a mammal in need
27 thereof of a therapeutically effective amount
28 of a) a specific binding member which binds to
29 a cell death receptor or a nucleic acid
30 encoding said binding member and (b) a
31 chemotherapeutic agent, wherein said
32 chemotherapeutic agent is a topoisomerase

1 inhibitor or a thymidylate synthase inhibitor.

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4 11. The method according to claim 9 or claim 10
5 wherein the cancer is one or more of
6 colorectal, breast , ovarian, cervical,
7 gastric, lung, liver, skin and myeloid (e.g.
8 bone marrow) cancer.

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10 12. The method according to claim 9, 10 or 11
11 wherein the binding member is an antibody or a
12 fragment thereof.

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14 13. The method according to any one of claims 9 to
15 12 wherein the death receptor is FAS.

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17 14. The method according to any one of claims 9 to
18 13 wherein the binding member is the anti-FAS
19 antibody CH11.

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21 15. The method according to any one of claims 9 to
22 14 wherein said chemotherapeutic agent is an
23 antifolate thymidylate synthase inhibitor or a
24 topoisomerase-I inhibitor.

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26 16. The method according to any one of claims 9 to
27 15 wherein, wherein said chemotherapeutic agent
28 is TDX or irinotecan (CPT-11) .

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30 17. The method according to claim 16 wherein said
31 specific binding member and chemotherapeutic
32 agent are provided in concentrations sufficient

1 to produce an RI of greater than 1.5.

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3 18. A product comprising a) a specific binding
4 member which binds to a cell death receptor or
5 a nucleic acid encoding said binding member and
6 (b) a chemotherapeutic agent as a combined
7 preparation for the simultaneous, separate or
8 sequential use in the treatment of cancer,
9 wherein said chemotherapeutic agent is a
10 topoisomerase inhibitor or a thymidylate
11 synthase inhibitor, and wherein the cancer
12 cells comprise a p53 mutation.

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14 19. A pharmaceutical composition characterised by
15 the presence of a p53 mutation, wherein the
16 composition comprises a) a specific binding
17 member which binds to a cell death receptor or
18 a nucleic acid encoding said binding member and
19 (b) a chemotherapeutic agent, wherein said
20 chemotherapeutic agent is a topoisomerase
21 inhibitor or a thymidylate synthase inhibitor
22 and (c) a pharmaceutically acceptable
23 excipient, diluent or carrier..

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25 20. The product according to claim 18 or the
26 pharmaceutical composition according to claim
27 19 wherein the cancer is one or more of
28 colorectal, breast , ovarian, cervical,
29 gastric, lung, liver, skin and myeloid (e.g.
30 bone marrow) cancer.

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- 1 21. The product according to claim 18 or claim 20
2 or the pharmaceutical composition according to
3 claim 19 or claim 20 wherein the binding member
4 is an antibody or a fragment thereof.
- 5
- 6 22. The product according to claim 18 or claim 20
7 or 21 or the pharmaceutical composition
8 according to claim 19 or claim 20 or 21 wherein
9 the death receptor is FAS.
- 10
- 11 23. The product according to claim 18 or any one of
12 claims 20 to 22 or the pharmaceutical
13 composition according to claim 19 or or any one
14 of claims 20 to 22 wherein the binding member
15 is the anti-FAS antibody CH11.
- 16
- 17 24. The product according to claim 18 or any one of
18 claims 20 to 23 or the pharmaceutical
19 composition according to claim 19 or or any one
20 of claims 20 to 23 wherein said
21 chemotherapeutic agent is an antifolate
22 thymidylate synthase inhibitor or a
23 topoisomerase-I inhibitor.
- 24
- 25 25. The product according to claim 18 or any one of
26 claims 20 to 24 or the pharmaceutical
27 composition according to claim 19 or or any one
28 of claims 20 to 24, wherein said
29 chemotherapeutic agent is TDX or irinotecan
30 (CPT-11).
- 31

1 26. The product or pharmaceutical composition
2 according to claim 25 wherein said specific
3 binding member and chemotherapeutic agent are
4 provided in concentrations sufficient to
5 produce an RI of greater than 1.5.

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7 27. A kit for the treatment of a cancer
8 characterised by the presence of a p53
9 mutation, said kit comprising a) a specific
10 binding member which binds to a cell death
11 receptor or a nucleic acid encoding said
12 binding member and (b) a chemotherapeutic
13 agent, wherein said chemotherapeutic agent is a
14 topoisomerase inhibitor or a thymidylate
15 synthase inhibitor and (c) instructions for the
16 administration of (a) and (b) separately,
17 sequentially or simultaneously.

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